

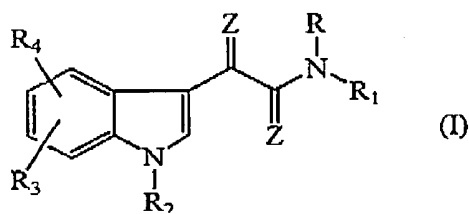
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 Client/Matter: 017094-0306034

# IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-13 (cancelled)

14. (New) A method of treating resistant tumors, metastasizing tumors, or tumors sensitive to angiogenesis inhibitors, comprising administering to a patient in need thereof, an effective amount of one or more N-substituted indol-3-glyoxylamides of formula 1, their physiologically tolerable acid addition salts, and N-oxides thereof

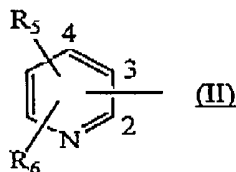


where the radicals R, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and Z have the following meaning:

R is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)-alkyl, where the alkyl group can be mono- or polysubstituted by a phenyl ring wherein the phenyl ring can be mono- or polysubstituted by halogen, (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>3</sub>-C<sub>7</sub>)-cycloalkyl, carboxyl groups, carboxyl groups esterified with C<sub>1</sub>-C<sub>6</sub>-alkanols, trifluoromethyl groups, hydroxyl groups, methoxy groups, ethoxy groups, benzyloxy groups and a benzyl group which is mono- or polysubstituted in the phenyl moiety by (C<sub>1</sub>-C<sub>6</sub>)-alkyl groups, halogen atoms or trifluoromethyl groups, or

R is a tertiary-butoxycarbonyl radical or an acetyl group;

R<sub>1</sub> is a phenyl ring, which is mono- or polysubstituted by (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>1</sub>-C<sub>6</sub>)-alkoxy, cyano, halogen, trifluoromethyl, hydroxyl, benzyloxy, nitro, amino, (C<sub>1</sub>-C<sub>6</sub>)-alkylamino, (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino, a carboxyl group, a carboxyl group esterified with C<sub>1</sub>-C<sub>6</sub>-alkanols, or a pyridine structure of formula 2 and its N-oxide



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where the pyridine structure is bonded at either the 2, 3 or 4 positions of the ring, and wherein  $R_5$  and  $R_6$  can be identical or different and are (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>3</sub>-C<sub>7</sub>)-cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)-alkoxy, nitro, amino, hydroxyl, halogen, trifluoromethyl, an ethoxycarbonylamino radical and a carboxyalkyloxy group in which the alkyl group of the carboxyalkyloxy has 1-4 C atoms, or

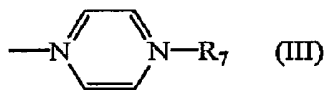
$R_1$  is a 2- or 4-pyrimidinyl heterocycle, where the 2-pyrimidinyl ring can be mono- or polysubstituted by a methyl group; a 2-, 3-, 4-, or 8-quinolyl, wherein the quinolyl structure may be substituted by (C<sub>1</sub>-C<sub>6</sub>)-alkyl, halogen, a nitro group, an amino group, and a (C<sub>1</sub>-C<sub>6</sub>)-alkylamino radical; a 2-, 3-, or 4-quinolylmethyl, where the ring carbons of the pyridylmethyl radical of the quinolyl group and of the quinolylmethyl radical can be substituted by (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>1</sub>-C<sub>6</sub>)-alkoxy, nitro, amino and (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino, or

$R_1$ , in the case in which R is hydrogen, a methyl group, a benzyl group, a benzyloxycarbonyl radical, a tert-butoxycarbonyl radical, or an acetyl group, can further be a radical selected from the group consisting of —CH<sub>2</sub>COOH; —CH(CH<sub>3</sub>)-COOH; (CH<sub>3</sub>)<sub>2</sub>CH-(CH<sub>2</sub>)<sub>2</sub>-CH-COO—; H<sub>3</sub>C-H<sub>2</sub>C-CH(CH<sub>3</sub>)-CH(COOH)—; HO-H<sub>2</sub>C-CH(COOH)—; phenyl-CH<sub>2</sub>-CH(COOH)—; (4-imidazolyl)-CH<sub>2</sub>-CH-(COOH)—; HN=C(NH<sub>2</sub>)-NH-(CH<sub>2</sub>)<sub>3</sub>-CH(COOH)—; H<sub>2</sub>N-(CH<sub>2</sub>)<sub>4</sub>-CH(COOH)—; H<sub>2</sub>N-CO-CH<sub>2</sub>-CH-(COOH)—; and HOOC-(CH<sub>2</sub>)<sub>2</sub>-CH(COOH)—; or

$R_1$ , in the case in which R is hydrogen, a benzyloxycarbonyl radical, a tert-butoxycarbonyl radical, an acetyl group or a benzyl group, can further be the acid radical of a natural or unnatural amino acid, or

$R_1$  can be an allylamino-carbonyl-2-methylprop-1-yl group;

R and  $R_1$  can further form, together with the nitrogen atom to which they are bonded, the structure of formula 3



wherein  $R_7$  is an alkyl radical, a benzhydryl group, a bis-p-fluorobenzhydryl group, or a phenyl ring which can be mono- or polysubstituted by (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>1</sub>-C<sub>6</sub>)-alkoxy, halogen, a nitro group, an amino function and a (C<sub>1</sub>-C<sub>6</sub>)-alkylamino group;

$R_2$  is hydrogen or a (C<sub>1</sub>-C<sub>6</sub>)-alkyl group, where the alkyl group is mono- or polysubstituted by halogen and phenyl, which for its part can be mono- or polysubstituted by

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halogen, (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>3</sub>-C<sub>7</sub>)-cycloalkyl, carboxyl groups, carboxyl groups esterified with C<sub>1</sub>-C<sub>6</sub>-alkanols, trifluoromethyl groups, hydroxyl groups, methoxy groups, ethoxy groups, benzyloxy groups, a 2-quinolyl group and a 2-, 3- or 4-pyridyl group, wherein the 2-quinolyl and 2-, 3- or 4-pyridyl groups can both in each case be mono- or polysubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)-alkyl groups or (C<sub>1</sub>-C<sub>4</sub>)-alkoxy groups, or

R<sub>2</sub> is an aroyl radical, where the aryl moiety on which this radical is based is a phenyl ring, which can be mono- or polysubstituted by halogen, (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>3</sub>-C<sub>7</sub>)-cycloalkyl, carboxyl groups, carboxyl groups esterified with C<sub>1</sub>-C<sub>6</sub>-alkanols, trifluoromethyl groups, hydroxyl groups, methoxy groups, ethoxy groups or benzyloxy groups;

R<sub>3</sub> and R<sub>4</sub> can be identical or different and are hydrogen, (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>3</sub>-C<sub>7</sub>)-cycloalkyl, (C<sub>1</sub>-C<sub>6</sub>)-alkanoyl, (C<sub>1</sub>-C<sub>6</sub>)-alkoxy, halogen, benzyloxy, a nitro group, an amino group, a (C<sub>1</sub>-C<sub>4</sub>)-mono or dialkyl-substituted amino group, a (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino function, or a (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino-(C<sub>1</sub>-C<sub>6</sub>)-alkyl function; and

Z is O or S;

15. (New) The method according to claim 14, wherein the amino acid is selected from the group consisting of a  $\alpha$ -glycyl, a  $\alpha$ -sarcosyl, a  $\alpha$ -alanyl, a  $\alpha$ -leucyl, a  $\alpha$ -isoleucyl, a  $\alpha$ -seryl, a  $\alpha$ -phenylalanyl, a  $\alpha$ -histidyl, a  $\alpha$ -prolyl, a  $\alpha$ -arginyl, a  $\alpha$ -lysyl, a  $\alpha$ -asparagyl and a  $\alpha$ -glutamyl radical, where the amino groups of the respective amino acids can be present unprotected or can be protected.

16. (New) The method according to claim 15, wherein the amino groups are protected by a carbobenzoxy radical, a tert-butoxycarbonyl radical, or an acetyl group.

17. (New) The method according to claim 15, wherein the amino acid is an asparagyl or a glutamyl radical, and the second, unbonded carboxyl group is present as a free carboxyl group or an ester of a C<sub>1</sub>-C<sub>6</sub>-alcohol.

18. (New) The method of claim 14, wherein R is hydrogen; R<sub>1</sub> is 4-pyridyl or 4-fluorophenyl; R<sub>2</sub> is benzyl, 4-chlorobenzyl, 4-fluorobenzyl, 3-pyridylmethyl, 4-bromobenzyl; R<sub>3</sub> and R<sub>4</sub> are hydrogen; and Z is oxygen.

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19. (New) The method of claim 14, wherein one or more of the N-substituted indol-3-glyoxylamides are selected from the group consisting of N-(pyridin-4-yl)-[1-(4-fluorobenzyl)indol-3-yl] glyoxylamide; N-(pyridin-4-yl)-(1-benzylindol-3-yl) glyoxylamide; N-(4-fluorophenyl)-[1-(3-pyridylmethyl)indol-3-yl] glyoxylamide; N-(pyridin-4-yl)-[1-(4-chlorobenzyl)indol-3-yl] glyoxylamide; N-(pyridin-4-yl)-[1-(4-fluorobenzyl)indol-3-yl] glyoxylamide, their physiologically tolerable acid-addition salts and N-oxides thereof.

20. (New) The method according to claim 14, wherein acid addition salt is a salt of a mineral acid or a salt or an organic acid.

21. (New) The method according to claim 20, wherein the salts of mineral acids are selected from the group consisting of hydrochloric acid, sulfuric acid, and phosphoric acid, and the salts of organic acids are selected from the group consisting of acetic acid, lactic acid, malonic acid, maleic acid, fumaric acid, gluconic acid, glucuronic acid, citric acid, embonic acid, methanesulfonic acid, trifluoroacetic acid, succinic acid, and 2-hydroxyethanesulfonic acid.

22. (New) The method according to claim 14, wherein physiologically tolerable N-oxide is any chemically possible N-oxide of an N-substituted indol-3-glyoxylamide or an acid addition salt thereof.

23. (New) The method according to claim 14, wherein the resistant tumor is a tumor at least resistant to an antitumor drug selected from the group consisting of taxol, doxorubicine, vincristine, and epotholone B.

24. (New) The method of claim 14, wherein the one or more N-substituted indol-3-glyoxylamides are used by themselves, in combination with one or more known antitumor agents, or as a replacement for one or more known antitumor agents which are no longer active on account of resistance formation.

25. (New) The method of claim 24, wherein the antitumor agent used in combination with the one or more N-substituted indol-3-glyoxylamides is selected from the group consisting of taxol, doxorubicine, vincristine, and epotholone B.

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26. (New) The method of claim 24, wherein the antitumor agent for replacement by one or more N-substituted indol-3-glyoxylamides is selected from the group consisting of taxol, doxorubicine, vincristine, and epotholone B.

27. (New) The method according to claim 25, wherein the one or more N-substituted indol-3-glyoxylamides and the one or more antitumor agents further comprise a pharmaceutically utilizable vehicle, diluent, or excipient.

28. (New) The method according to claim 27, wherein the one or more N-substituted indol-3-glyoxylamides, the one or more antitumor agents, and the pharmaceutically utilizable vehicle, diluent, or excipient is in the form of a tablet, coated tablet, capsule, solution for infusion or ampoule, suppository, patch, powder preparation which can be employed by inhalation, suspension, cream, or ointment.

29. (New) The method of claim 26, wherein the N-substituted indol-3-glyoxylamide is selected from the group consisting of N-(pyridin-4-yl)-[1-(4-fluorobenzyl)indol-3-yl] glyoxylamide; N-(pyridin-4-yl)-(1-benzylindol-3-yl) glyoxylamide; N-(4-fluorophenyl)-[1-(3-pyridylmethyl)indol-3-yl] glyoxylamide; N-(pyridin-4-yl)-[1-(4-chlorobenzyl)indol-3-yl] glyoxylamide; N-(pyridin-4-yl)-[1-(4-fluorobenzyl)indol-3-yl] glyoxylamide, their physiologically tolerable acid-addition salts and N-oxides thereof.